

Towards a completely implantable, light-sensitive intraocular retinal prosthesis.

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I. Introduction.

An electronic retinal prosthesis is under development to treat retinitis pigmentosa and age-related macular degeneration, two presently incurable diseases of the outer retina that afflict millions worldwide. Previous studies have established the feasibility of the retinal prosthesis. Short-term tests in blind humans have shown that degenerated retina will respond to light in a way that is consistent with form vision [1]. Post-mortem analysis of human eyes with RP and AMD show a significant survival of inner retinal cells despite near complete degeneration of the photoreceptors in the outer retina [2]. Long-term implants have demonstrated that the retina can tolerate the physical presence of an electrode array without degenerating due to pressure or other mechanical affects [3].

The focus now has turned towards the development of a chronic stimulator [4]. Initial prototypes based on current technology will have a small number of pixels and will place the stimulation electronics outside the eye. However, more advanced devices are in the early development stages. A completely implantable, light-sensitive retinal prosthesis must include capability for both phototransduction and stimulus current generation, two power intensive functions. These devices will be implanted in the eye, creating a significant source of heat that must be dissipated by the ocular tissue without

damaging the retina. Therefore, it is imperative to obtain a good understanding of the power dissipation properties of the eye to guide the development of such a chip. Future prosthesis must also have a high density electrode array with over 1000 contacts, in order to be restore any useful vision to blind individuals. An electrode structure that can interface a flat chip to the curved retina would have distinct advantages over silicon or polyimide arrays, where material strength and routing of conducting lines may be problematic. While other technological barriers do exist to a completely implanted, light-sensitive retinal prosthesis, heat tolerance and high-density electrodes have been the focus of recent activity.

II. Methods

Heat Experiments - A custom, intraocular heater apparatus was constructed to apply 0, 10, 20, 50, 100, 200, or 500 mW via a 1.4x1.4x1 mm resistor. The heater probe was instrumented with 2 thermocouples: one on the heater and a second on the probe cable, 6 mm away. The heater probe was inserted into the vitreous cavity and power was applied. Two heater positions were tested: retinal and mid-vitreous. Dogs were used in these experiments following an approved protocol. An initial experiment was followed for weeks later by a second, identical

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experiment in the fellow eye, yielding acute and chronic damage data from a single animal. Electroretinography, fundus photography, and histology were used to determine the health of the retina after heating.

High Density Electrode Array –

Nanoscale wires were formed in porous substrates to serve as the basis for a retinal stimulating array. Channel glass is an electrically insulating material that forms pores with high aspect ratios. Glass can be polished to match the curvature of the retina. Channel glass is fabricated using glass drawing procedures that involve bundled stacks of composite glass fibers[5]. The process begins by placing an acid-etchable glass rod into an inert glass tube and drawing this pairing of dissimilar glasses at elevated temperature into a fiber of smaller diameter. Several thousand of these fibers are then cut and stacked in a hexagonal-close-packed arrangement, yielding a hexagonal-shaped bundle. This bundle is subsequently drawn at elevated temperature, fusing the individual composite fibers together while reducing the overall bundle size. At this stage, the fibers are hexagonal shaped and contain a fine structure of several thousand micron-sized (typically 5 to 10 micron diameter) acid etchable glass fibers in a hexagonal-close-packed pattern. Standard microchannel plate glass is obtained at this point by bundling these fibers together in a twelve-sided bundle and fusing the bundle together at elevated temperature. Alternatively, nanochannel glass may be obtained by stacking the hexagonal shaped fibers into a new bundle and then drawing the bundle at elevated temperature, thereby fusing the individual fibers together and reducing the overall size. In this

manner, submicron channel diameters and extremely high channel densities can be achieved. After the last glass draw, the boules are wafered, polished and then etched to remove the acid etchable glass. In this way, a glass with extremely uniform, parallel, hollow channels is obtained.

Conductors are formed in the porous substrates by sputtering one side of the porous material, attaching a lead wire to the sputter side, and then exposing the other side of the porous material to plating solution. Wires of nickel, copper, and platinum were deposited.

An in depth study of platinum microstructure as related to plating potential was conducted. Platinum films were electrochemically deposited out of solution onto gold substrates using different deposition potentials. Electrochemical deposition was performed using a three-electrode setup consisting of a Au-Cr-Si working electrode (chromium sputtered on silicon followed by a superlayer of gold – chromium alleviates mechanical stresses between Au & Si so flaking does not occur), a platinum counter electrode and a Ag/AgCl (silver-silver chloride) reference electrode. A teflon open bottom chamber was clamped onto the working electrode and the cell was filled with 0.01667M ammonium hexachloroplatinate (IV) solution. This solution is different from standard platinum plating solution which contains lead acetate. The working electrode was inserted through the top of the cell and the reference electrode was placed inside the auxiliary Luggin capillary (small channel bored into the teflon to allow correct reference placement) built into the teflon cell. The system was

connected to a digital potentiostat controlled by PC.

Potentiostatic (constant potential vs. time) depositions were performed at 300, 400, 500, 600, 700 and 800mV potentials, each for two-hour intervals. Current was recorded vs. time for each 2-hour interval. Following each deposition, remaining solution was poured off, the cell was unclamped, and the sample was rinsed with distilled water. Compressed nitrogen was used to dry the samples.

III. Results

Heat Experiments. When the heater was positioned on the surface of the retina, 50mW or higher heater settings caused a immediate, visible damage to the retina. However, histologically, this damage was evident only if the eyes were immediately sacrificed and fixed (i.e., acutely studied). If the histology was performed 4 weeks later (i.e., studying the chronic effect), damage was only noted at 100mW or higher heater settings. When the heater was placed in the midvitreal cavity, no ophthalmological, ERG, or histological differences were noted. When 500 mW was applied, the thermocouple on heater reached temperatures of 77 – 87 deg. C, but obtained a steady state. A third thermocouple probe, in a hypodermic needle that could be positioned independently of the heater, was used to monitor the temperature of the retina, which was increased only 2-3 deg. C by 500 mW power dissipation. Likewise, the temperature at the thermocouple on the cable, 6 mm from the heater, was elevated much less than the heater. Fig. 1 shows the temperature at all three locations recorded during a two hour experiment.

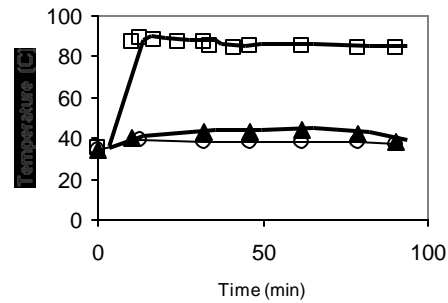


Figure 1 Heat in the eye during 90 minutes heating with 500 mW measured at the heater (square), the retina (triangle), and on the cable 6 mm from the heater.

High-Density electrode array. 40 micron platinum wires were formed in 5 micron pores (Figure 2). These appear to be high quality wires with no discontinuities. However, platinum plating occurs very slowly, creating difficulties in maintaining the integrity of the plating setup throughout the process. The process may last several hundred hours to achieve a 400 micron wire.

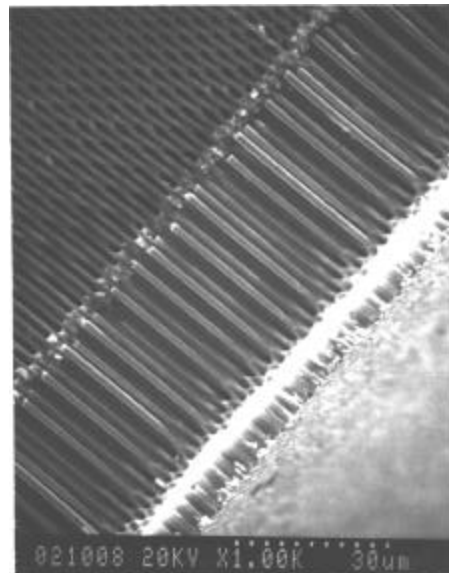


Figure 2 – 40 micron long platinum wires formed in 5 micron channels.

A study of the microstructure of plated platinum vs. potential revealed that a plating potential of -600 mV yielded a dendritic porous structure, while other potentials (-300 , -400 , -500 , -700 , and -800 mV) yielded platinum with a finer microstructure. The highest efficiency deposition was at -400 mV.

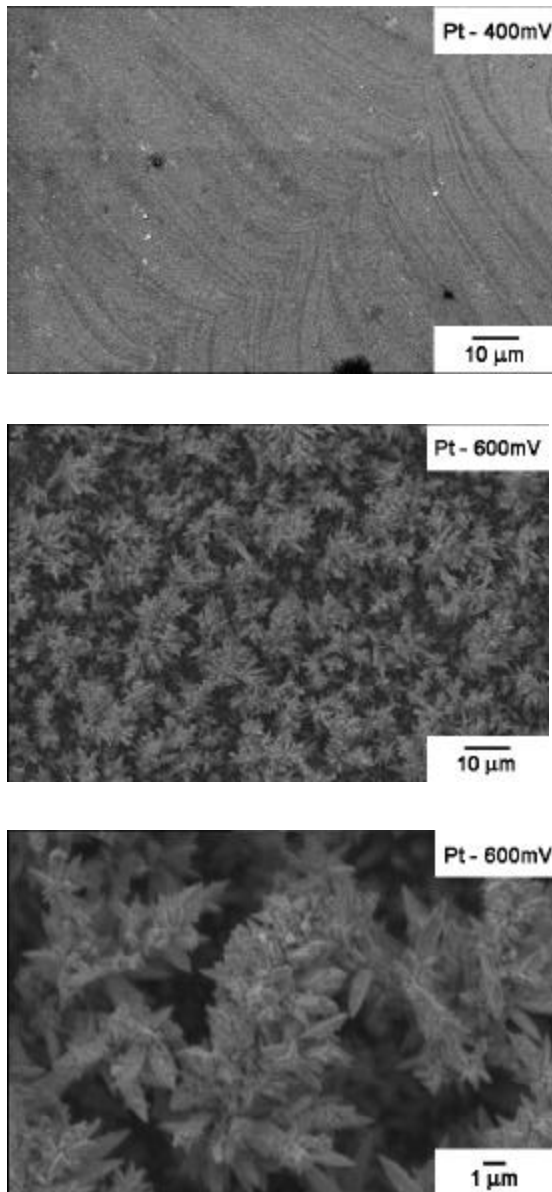


Figure 3 – Top platinum deposited at -400 mV showing a dense, smooth structure. Middle – platinum deposited at -600 mV has a dendritic structure, Bottom – higher magnification of dendritic platinum.

IV. Conclusion

Significant technological hurdles remain to developing a high-density, light-sensitive intraocular retinal prosthesis. The amount of heat that can be safely dissipated by the eye and surrounding head without harming the retina, depends significantly on the position of the heater. Technology for a high-density electrode array is advancing, but high-quality wires of biocompatible material in dimensions usable for a retinal prosthesis material have yet to be achieved.

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